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DIABETIC RETINOPATHY;

PREDICTIVE VALUE OF ELEVATED HBA1C LEVELS FOR THE PRESENCE OF DIABETIC RETINOPATHY

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ABSTRACT… Background: Diabetic retinopathy is one of the most common complications of diabetes affecting more than 1/4th of the diabetics and is also the leading cause of blindness in many parts of the globe. Regular fundoscopic examination for screening is a routine practice in tertiary care hospitals but is not available in the primary care centers. This necessitates the development of a reliable screening tool which will allow for early referral of those with complications to the specialist centers. **Objective:** To determine the predictive value of HbA1c levels for the presence of diabetic retinopathy. **Study Design:** A cross-sectional study. **Setting:** Diabetic Clinic of Mayo Hospital, Lahore. **Period:** 04 months, January to April 2017. **Method:** 75 diabetic patients who presented in Diabetic clinic were investigated for HbA1c levels and fundoscopic evaluation was done to detect retinal changes. **Results:** Out of 75 patients, 35 (46.7%) were female, 40 (53.3%) were male. Median age of the patients was 51 years. All patients had HbA1c levels more than 6.0% and 62% patients had detectable changes on fundi while the rest had no detectable retinal disease despite elevated HbA1c levels. Positive predictive value (PPV) of elevated HbA1c levels for the presence of diabetic retinal changes was calculated to be 62.66%. **Conclusion:** All the patients who had retinal disease on fundoscopy had HbA1c levels of more than 6.0% (PPV = 62.66) which means that elevated HbA1c levels warrant a fundoscopic retinal examination to rule out diabetic retinopathy.

Key words: Diabetic retinopathy, Fundoscopy, HbA1c, Screening.

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INTRODUCTION

Diabetes Mellitus is defined as a group of metabolic disorders which are characterized by hyperglycemia, and may be due to either insulin deficiency or abnormal insulin function, which have widespread micro-vascular complications in eyes, kidneys, nerves, hearts and blood vessels.[1] A 1998 projection of WHO data said that 4% of world population or 135 million people were diabetic, which were estimated to rise to 5.4% or 300 million by 2025. The projection also suggested that most raise would be indigenous to developed countries.[2] The 2016 WHO global report on diabetes showed an alarming quadrupling of diabetics from 1980 to 422 million in 2016, a number higher than the previous projections, and that too about ten years prior to the estimate.[3] The Diabetes Control and Complications Trial / Epidemiology of Diabetes Interventions and Complications trial (DCCT/EDIC) elucidated the importance of early diabetes control and ear-marked a 76 % reduction in eye complications (retinopathy) with good and early diabetes control.[4]

Diabetic Retinopathy (DR) (the micro-angiopathic vascular complication of diabetes resulting in ischemia and leakage) is the leading cause of blindness in Western world and is one of the most common complications of diabetes.[3,5] More than 30% of the patients suffering from DM have diabetic retinopathy.[6] The racial and geographical factors vary in Pakistan much from the indigenous area of DCCT and the screening methods of NHS yield the patient at a much earlier stage of disease before the retinopathy sets in. In Pakistan the presentation is quite late, depending upon the socio-economic and cultural as well as literacy variables. Beginning in-utero the low birth weight and gestational diabetes, along with specific

genetic make-up and environmental factors make the epidemiology of Diabetes very distinct in Pakistan, necessitating exhaustive research upon the context.[7] It also makes imperative that such patients be seen regularly, with strict follow-ups, something yet again not available in Pakistan. Diabetic retinopathy develops within about 5 years of onset of diabetes, so around 50% diabetics develop retinopathy in 10 years of onset of disease and 90% have the retinopathy after 30 years of being diabetic.[8] Owing to insidious initial course of diabetic retinopathy patients often present later in the proliferative stages of retinopathy, at times with center threatening diabetic macular edema, when more often than not the damage is already done. There is hence a need for developing a diagnostic tool, which is sensitive enough to detect the altered blood glycemic levels and specific enough to not allegedly point out diabetic status and hence directing for regular fundal examination.

Glycated Hemoglobin or HbA1c for short can be pruned to be one such tool. It can be tested at one point in time on patient's presentation in diabetic clinic, and if found deranged it reflects the blood glucose levels over a period of past 3 months. However, it has not yet been declared the diagnostic test of choice despite being the gold standard.[9] Current clinical practice guidelines recommend HbA1c of less than 6.5%, 7.0%, or 8.0%, depending on the agency and the individual patient's goals and clinical complexity.[10,11,12,13,14,15,16] The United Kingdom where the incidence of diabetes is 7.7%[17], the incidence of Diabetic Retinopathy is 23.1% of all type 2 diabetics[18], with provision of HbA1c testing and dilated fundus examination along with availability of insulin as well as oral hypoglycemic drugs and retinal photocoagulation at primary care facilities. In comparison, in Pakistan 9.8% population is diabetic and the incidence of retinopathy amongst them have been recorded at various centers to be 15.62%, 26% and 51.61%, with no provision of either of the above mentioned screening and/or therapeutic tools available at the primary care facilities.[19-22] Furthermore, the information furnished by the patients about glycemic control is unreliable with 75% of complicated diabetics claiming a good control.[19] Hence HbA1c testing which may be regarded as over-zealous and prone to making a stringent treatment plan for patients in UK[23], is seen to be a necessity in the settings of Pakistan for ascertainment of diabetic control, and for referring the patient from primary care to tertiary care for fundal exam and intervention.

METHODS

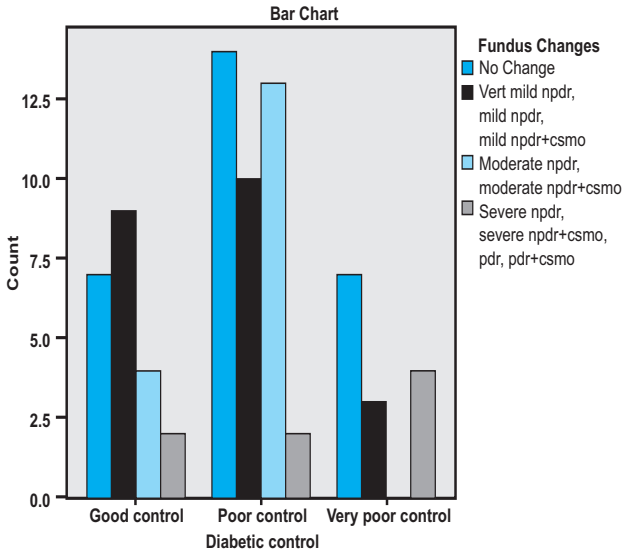
A cross sectional study design in which 75 patients suffering from type 2 diabetes who presented to Diabetic Clinic of Mayo Hospital Lahore were selected randomly by non-probability consecutive sampling. The patients underwent a dilated fundal examination using Indirect Ophthalmoscopy. The fundal findings were recorded using the International Clinical Disease Severity Scale for Diabetic Retinopathy.[24] Blood samples taken in the same sitting were examined at one laboratory for HbA1c levels. Random blood sugar levels were measured. After taking informed consent, data was compiled using a simple pro-forma. Data analysis was done using SPSS 23.

RESULTS

Out of 75 patients, 35 (46.7%) were female, 40 (53.3%) were male. Median age for the patients was 51 years. Duration of diabetes for most patients was found to be under 15 years (94.7%), with only 2 (2.7%) patients having duration of 20 years and 1(1.3%) each 25 and 28 years. 61 patients (81.3%) were using oral hypoglycemic drugs while 11 patients (14.7%) were injecting Insulin. 4 % people were taking both oral drugs and injecting insulin.

Mean HbA1c levels were 8.9% (n=75 SD1.3816). All the patients had HbA1c levels of 6.0% or more. Out of 75 patients 28 patients (37.33%) had no observable diabetic changes on their fundi, despite having HbA1c values in the abnormal range. 22 patients had mild NPDR out of whom one had Centre threatening Diabetic Macular Edema-DME (previously known as CSME). 17 patients (22.7%) had moderate NPDR with 8 patients having DME. 4 out of 5 patients (6.66%) of severe NPDR also had Centre threatening DME. 3 patients had Proliferative stage of DR. Positive predictive value of elevated HbA1c levels

was calculated to be 62.66% (p-value < 0.05 (Figure-A). 19.4% patients had Random Blood Sugar (BSR) levels below 200mg/dl. Mean BSR level was 290 mg/dl with a SD of 85 (n=72).



DISCUSSION

The idea behind the screening for diabetic retinopathy is that if diagnosed and managed at an early stage, outcome is much better. There are many options for treating DR but strict long-term diabetic control is the most important one. Other options include laser photocoagulation, intravitreal injections of steroids and anti-VEGF.[25] Current guidelines recommend annual fundoscopic examination in a patient with no evidence of DR and more frequent examinations in the diagnosed cases of DR.[25] Pakistan is a country with limited resources. Not all the diagnostic and therapeutic facilities for diagnosis and management of diabetic retinopathy are available at the primary care facilities. In a setting where fundoscopic examination is not available at the primary care, the next question is that which patients are at high risk of having DR and who should be referred for further evaluation apart from the symptomatic ones.

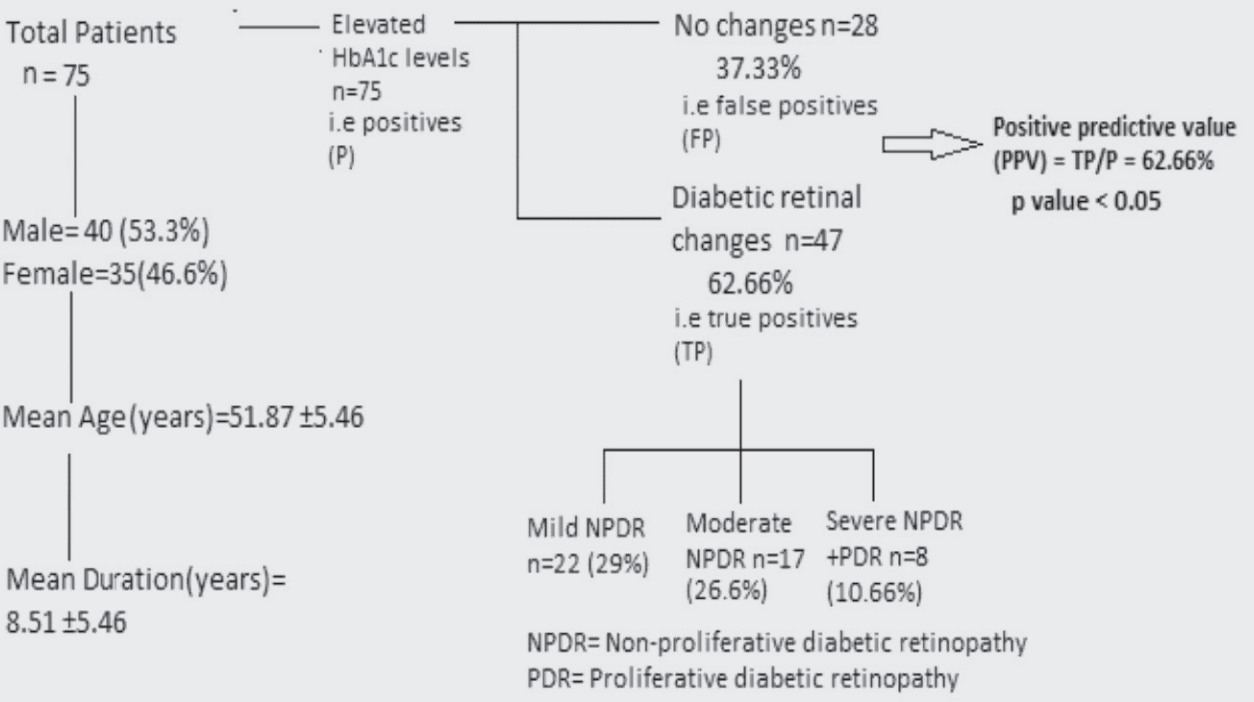


Fig.A

In order to answer this question an attempt was made to find out the correspondence of findings of diabetic retinopathy changes on fundi of people with diabetes and their HbA1c levels since it indicates chronic glycemic control.[9] In 100% of the patients with diabetic changes on fundi, HbA1c levels were found to be above 6.0%. Whereas Random blood sugar levels were found to be below the 200 mg/dl cut-off value in 20% of the patients who had detectable changes on their fundi. Hence the Random blood sugar profiles could possibly miss the presence of vision threatening complications of diabetes on eye, whilst HbA1c levels are found abnormal if the glycemic control is insufficient. As HbA1c levels were always found to be deranged in patients with positive changes for DR, it is safe to hazard the guess that a diabetic patient with deranged HbA1c levels qualifies for a fundal examination by a certified ophthalmologist with Indirect Ophthalmoscopy.

CONCLUSION

Using HbA1c levels will circumvent the unnecessary fundal exams and loss of patients to long follow-ups, while at the same time will ensure that any patient at high risk of diabetic retinopathy is not missed because of a misleadingly normal random blood sugar profile.

Limitations of this Study and Suggestions for Future Researches

Some patients were known diabetic for small duration while other were known diabetics for many years. The predictive value of HbA1c at the time of diagnosis, early and late in the course of the disease remains to be studied separately.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Samreen Hameed	Significantly contrubuted to literature review, manuscript writing discussion, conclusion and final review of the paper.	
3	M. Sultan Ul Moazzam	Significantly contrubuted to literature review, manuscript writing discussion, conclusion and final review of the paper and provide correspondence for the article.	
4	Sarmad Zahoor	Significantly contrubuted to literature review, manuscript writing discussion, conclusion and final review of the paper.	
5	Sidrah Latif	Significantly contrubuted to literature review, manuscript writing discussion, conclusion and final review of the paper.	
6	Mr. Yasir Bashir	Significantly contrubuted to literature review, manuscript writing discussion, conclusion and final review of the paper.	